Pulmonary Granulomatosis Associated with Excessive Use of Cosmetic Sprays

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LITTLE REFERENCE has been made in the medical literature to the possibility that pulmonary granulomatosis may be associated with the use of cosmetic or astringent sprays on the hair or body. In March of 1958, Bergmann and coworkers,[1] reporting on observations in two patients, suggested that hair sprays are not altogether harmless. Both of the patients were women in their twenties. One of them had been using various hair sprays for about two years, the last six months of which she had been in the habit of spraying her hair twice daily. The second patient had been using hair spray daily for three years. In both cases x-ray films showed extensive and widespread infiltrative changes, and there were surprisingly few associated respiratory signs or symptoms in either patient. In both instances the roentgenographically visible lesions disappeared spontaneously about three months after discontinuation of the use of hair spray.

In one patient, the microscopic finding of para-aminosalicylic acid-positive cytoplasmic inclusions in the histiocytic granulomatous infiltrate of a biopsy specimen of a scalene node convinced Bergmann and his associates that the lesion was distinctly different from those of sarcoidosis. This discovery stimulated them to study the effects following subcutaneous injections of a residue suspension from a well known brand of hair spray into the inguinal regions of three guinea pigs. Microscopic study of the lesions produced in all three animals revealed the characteristic para-aminosalicylic acid-positive granules in foam cells scattered throughout the granulomatous process. From this finding and other microscopic changes they concluded that the injected hair-spray residue acted like a typical macromolecular substance.

Bergmann[2] said that since the publication of their article in 1958, they have seen similar conditions in a number of cases, which are to be reported.

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In the following case the history, the physical findings, the radiographic changes and the results of tissue examination were strikingly like those in the two cases reported by Bergmann and coworkers.

REPORT OF A CASE

The patient, a 29-year-old woman, was admitted to the Santa Barbara General Hospital on June 1, 1959, because of extensive bilateral lung lesions, somewhat suggestive of tuberculosis, observed on a routine radiograph of the chest (Figure 1) taken May 29, 1959, as part of a gynecologic examination. A routine 70 mm. minifilm (Figure 2) taken May 1, 1957, showed no such changes. A 14x17 film taken on June 11, 1959, and a right lateral film (Figure 3) showed the same extensive bilateral symmetrical pulmonary infiltration of multicentric configuration.

The patient was employed as a nurses' aide at another hospital. On admission she had no significant symptoms referable to the respiratory tract and considered herself to be in good health. She said she frequently danced for an entire evening without feeling short of breath, and her weight had remained constant at 110 to 113 pounds since 1956.

In January of 1959 she had a mild upper respiratory tract infection of two weeks' duration, characterized by hoarseness, slight productive cough and fever not exceeding 99.8° F.

On specific questioning (after a pathologic report on biopsy material indicated this line of questioning) she said that she had been using various body, room and hair sprays since 1954. Between 1957 and 1959 she used five different cosmetic sprays extensively and concurrently. She was in the habit of spraying her body daily after bathing, and on returning from work, she invariably sprayed her room heavily with cologne.

No significant abnormalities were observed on physical examination. Response to a skin test with tuberculin intermediate strength purified protein derivative was negative; with a second strength PPD it was 2-plus at the end of 48 hours. Results of tests with histoplasmin and coccidioidin in various dilutions were negative. Results of urinalysis, blood cell counts and hematocrit and hemoglobin determinations were all within normal limits, as were serum calcium, total and fractional serum protein, alkaline phosphorus and nonprotein nitrogen and the results of a bromsulfthalein test. The erythrocyte

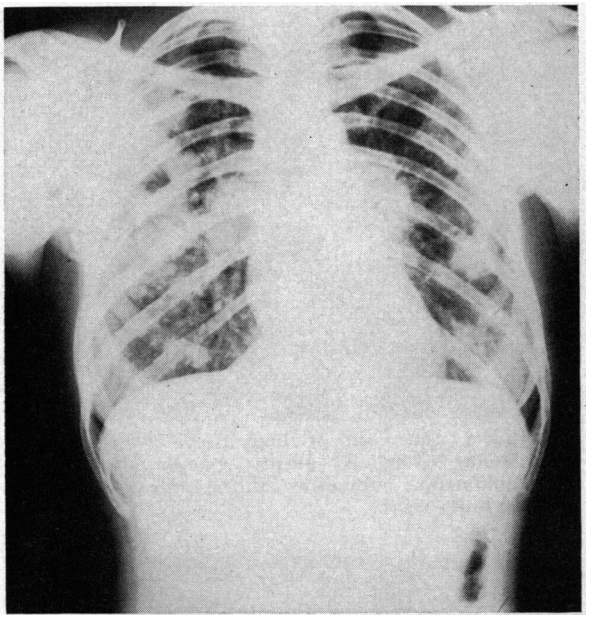

Figure 1.—Routine chest roentgenogram obtained on May 29, 1959, two days before admission to the hospital, showing extensive and diffuse bilateral granulomatous infiltrate. The patient was asymptomatic.

sedimentation rate (Wintrobe) was 32 mm. in one hour and remained rapid throughout the hospital stay. The result of a cephalin flocculation test was 2-plus at 24 hours and 4-plus at 48 hours; and results were the same later during the time the patient remained in the hospital. Fourteen consecutive 24-hour sputum specimens were negative for acid-fast bacilli on slides and culture, as were three specimens of gastric washings. Three fresh sputum specimens submitted for culture for predominating organisms were negative for pathogenic forms. However, the patient had very little sputum for examination.

The patient received no antibiotics or antituberculous drug therapy at the beginning of the period in hospital. Because of the response to the tuberculin test and the radiographic observations, it was decided to keep her under observation in the hospital. On June 17, 1959, her temperature was 103° F. for a 24-hour period and she complained of a severe sore throat. The vessels of the pharynx were decidedly engorged. The patient was given 400,000 units of penicillin-V by mouth five times daily and 250 mg. of oxytetracycline four times daily for five days. At the end of this period the pharyngeal symptoms had subsided and the temperature had returned to normal. X-ray films of the chest taken July 23, July 31 and August 20 showed no change. Films of the hands and feet, taken June 15, showed no abnormality.

Results of ventilatory function studies carried out in June and July, 1959, were within normal limits.

Biopsy of a specimen of scalene lymph node on June 18 showed noncaseating granulomatous lymphadenitis (Figure 4). The pathologic report on a

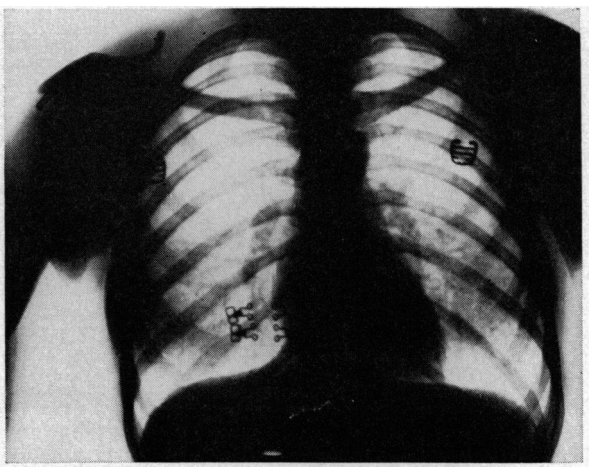

Figure 2.—Photograph of a 70 mm. minifilm obtained on May 1, 1957. This radiogram was interpreted as being within normal limits.

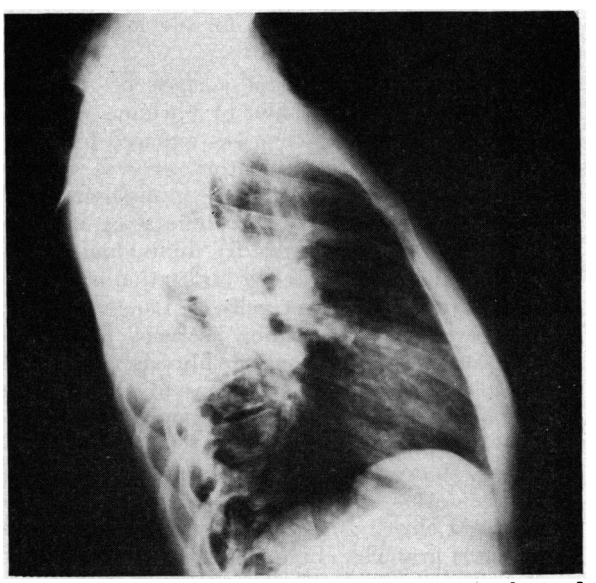

Figure 3.—Right lateral chest roentgenogram obtained on June 11, 1959. This film shows the distribution of the infiltrates and the apparently normal upper mediastinum.

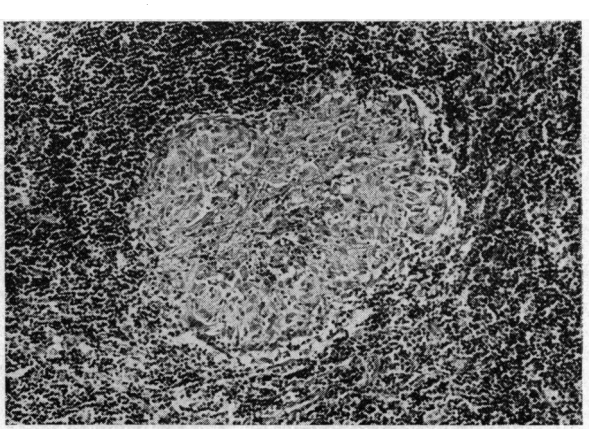

Figure 4.—Scalene lymph node (hematoxylin and eosin stain, reduced from ×450). Noncaseating granulomatous focus associated with bilateral pulmonary granulomatosis.

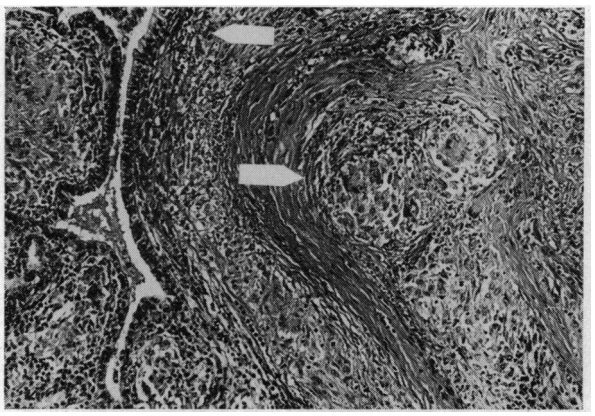

Figure 5.—Specimen of lung tissue (hematoxylin-eosin stain, reduced from ×450), showing pulmonary granulomatosis. Peribronchial infiltrate (arrow, left) and confluent granulomatous foci with marginal fibrosis (arrow, right).

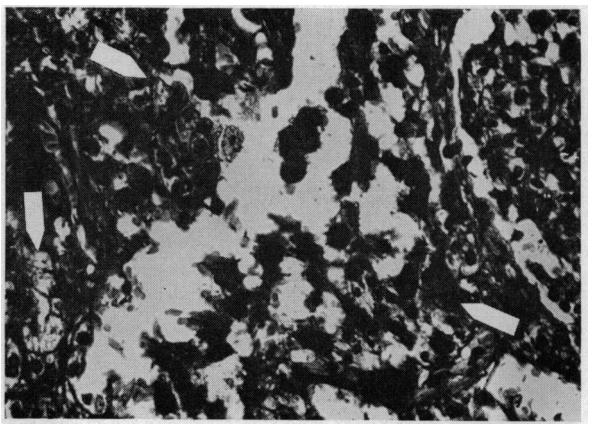

Figure 6.—Specimen of lung tissue (periodic acid-Schiff stain, ×970). PAS-positive cytoplasmic inclusions in granulomatous pulmonary infiltrate, obscuring nuclear detail at lower right.

specimen of lung tissue taken for biopsy August 17 follows:

"*Microscopic.* The pleural surface of the lung was covered with a thin film of fibrinous exudate. The pulmonary parenchyma was replaced by a diffuse granulomatous inflammatory process characterized by the presence of multiple granulomata that were confluent in many areas, obliterating the normal alveolar pattern (Figure 5). Individual granulomata showed epithelioid cell infiltration and occasional multinucleate giant cells of Langhans type, with no evidence of caseation necrosis. There was slight interstitial pulmonary fibrosis. Terminal bronchioles and occasional groups of alveoli were dilated and filled with pooled eosinophilic pink material containing numerous histiocytes. Further examination showed cytoplasmic pink granules within many histiocytes. Periodic acid stains showed these to represent clusters of foam cells with PAS-positive cytoplasmic granules (Figure 6). Small numbers of similar phagocytes containing PAS-positive material were distributed throughout the granulomatous foci. No fungi were demonstrated. Acid-fast stains showed no acid-fast bacilli. Grocott stains for fungi are negative.

"*Diagnosis.* Pulmonary granulomatosis, consistent with 'hair-spray granuloma.'

"*Comment.* The microscopic appearance is identical with that produced experimentally by Bergmann and coworkers by subcutaneous injection of a well-known brand of hair-spray. Pulmonary infiltration is so extensive in the biopsy material that liver involvement is probable."

It was after this report was received that questioning of the patient brought to light the excessive exposure to spray-type cosmetics, and she was thereupon discharged from the hospital with advice to discontinue exposure to sprays. She returned to work as a nurses' aide and reported regularly to our outpatient chest clinic for follow-up examinations.

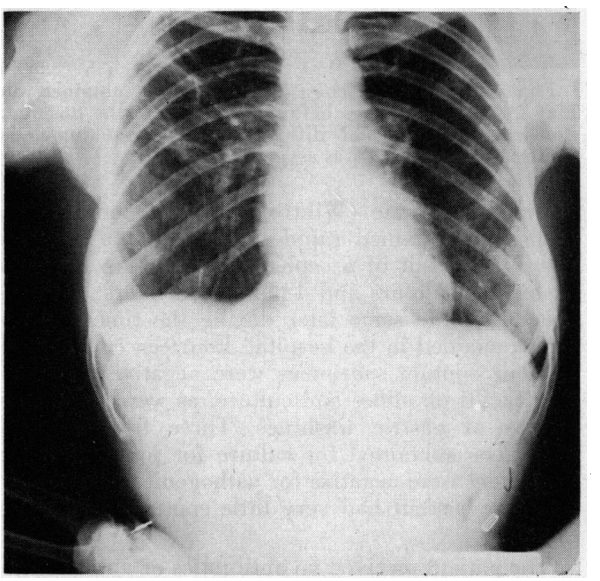

Figure 7.—Chest roentgenogram taken November 9, 1960, six months following the film shown in Figure 4. Note the dramatic clearing of the granulomatous infiltrates which took place between 12 and 18 months after the patient discontinued the use of body spray.

She was given no treatment and remained asymptomatic. X-ray films of the chest were taken from time to time and it was not until November, 1960, more than a year after the patient was discharged from the hospital, that significant diminution in the extensive pulmonary granulomatous process was shown (Figure 7).

The erythrocyte sedimentation rate still was above the normal range. However, the result of a cephalin flocculation test on February 1, 1961, was normal.

The patient remained well and continued to work. Ventilatory pulmonary function studies carried out February 1, 1961, were still essentially normal. The patient said she had not used cosmetic sprays for 21 months.

DISCUSSION

There is an element of uncertainty in suggesting that the pulmonary granulomatosis (thesaurosis) in this case was produced by the excessive use of body sprays. It is regrettable that qualitative tests for polyvinylpyrrolidone were not performed on the lung tissue removed for biopsy. Bergmann[2] said he considers this test necessary for an absolutely certain diagnosis, as he and his coworkers have apparently incriminated this ingredient by chemical analysis of various sprays as responsible for the changes evoked by prolonged inhalation.

The pathologic changes suggesting the diagnosis are shown in Figures 5 and 6. The lesion is practically indistinguishable microscopically from sarcoidosis except for the presence of the PAS-positive granules in the histiocytes. These granules were seen in all the cases Bergmann[2] observed. It is significant that we were unable to demonstrate similar PAS-positive granules in specimens from known cases of sarcoidosis selected from our pathologic files. In view of these observations, and in the absence of other possible etiologic agents, the history of excessive exposure to spray type cosmetics certainly seems more than coincidental.

It is noteworthy that in the present case more than a year elapsed before the pulmonary lesions cleared, whereas it took an average of only three months after discontinuance of sprays in the two cases originally reported by Bergmann.[1] Our impression following correspondence with Bergmann, however, is that the lung reaction in the present case was pathologically and radiographically more extensive and intensive than in most of the cases he observed.

The virtual complete resolution of the lesions on the radiograms is by no means specific for thesaurosis. However, this degree of resolution without steroid therapy would be regarded as most unusual in extensive pulmonary sarcoidosis, which in our opinion is now the only significant entity to be considered in the differential diagnosis.

Obviously more data must be accumulated regarding this probable entity before final conclusions can be drawn.

SUMMARY

In a case of diffuse bilateral pulmonary granulomatosis, the lesions disappeared without therapy approximately 14 months after the patient stopped using cosmetic body spray that she had previously used often. Scalene node biopsy and lung biopsy revealed a granulomatous reaction identical with that previously described following the use of hair spray. This factor should be considered in patients with asymptomatic pulmonary disease.

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REFERENCES

1. Bergmann, M.: Flance, I. J., and Blumenthal, H. T.: Thesaurosis following inhalation of hair spray, N.E.J.M., 258-471-476, 1958.

2. Bergmann, M.: Personal communication.

Hemolytic Disease of the Newborn Due to Sensitization to the Blood Factor hr'

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SINCE THE DISCOVERY of the hr' factor by Levine in 1941,[5] approximately 30 articles concerning hemolytic disease of the newborn due to sensitization to this factor have appeared in the literature.

In view of the relative infrequency of hemolytic disease of the newborn related to maternal sensitization to the hr' factor it seems important to report the following case.

REPORT OF A CASE

The patient, obese, 37 years of age, gravida IX, para V, abortus III, was admitted to Kern County (California) General Hospital on June 1, 1960. The expected date of confinement was June 17, 1960. None of her five living children, whose birth weights had ranged from 7 pounds to 9 pounds 8 ounces, had jaundice in the newborn period and all were well. In none of the three cases in which abortion occurred did gestation continue more than a few weeks and the cause of abortion was not known.

The patient had received three blood transfusions —January 25, 1950, after an abortion; September 27, 1957, and September 28, 1957, for postpartum hemorrhage. Since there was a family history of diabetes mellitus a glucose tolerance test was done May 27, 1960. The results were indicative of latent diabetes mellitus. A 1200-calorie diet was prescribed and the patient was observed regularly in the Diabetic Clinic. Blood sugar content remained within normal limits during that time.

On June 3 the patient was delivered of a 9-pound 3-ounce edematous girl with grayish-blue discoloration of the body that was attributed to a somewhat difficult delivery. Cyanosis of the face was also noted. Studies of the infant's blood done the next morning showed a positive reaction to a Coombs test; serum bilirubin of 23.7 mg. per 100 cc.; hemoglobin, 15.3 gm. per 100 cc.; hematocrit, 53 per cent; 3 nucleated red blood cells per 100 white blood cells. The blood was typed as Group O, Rh_0-positive, hr'-positive. The mother's blood was Group B, Rh_0-positive, hr'-negative. It was believed that the infant had hemolytic disease of the newborn due to maternal sensitization to the hr' factor. An exchange transfusion was done, using 500 cc. of Group O, Rh_0-positive, hr'-negative blood and the infant tolerated the procedure well. The bilirubin was 24.6 mg. per 100 cc. before the exchange and 13.6 mg. after it. On the morning of June 5, 1960 the bilirubin was 22.4 mg. per 100 cc. A second exchange transfusion was done, using 500 cc. of Group O, Rh_0-positive, hr'-negative blood, without incidence. The bilirubin content was 25.6 mg. per 100 cc. before and 14.6 mg. after the exchange. On the morning of June 6, 1960, the bilirubin was 21.4 mg. per 100 cc., the

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